In addition to disease and disablement during life, asbestosis has accounted for a large proportion of deaths among workers. The first reports of the disease (Auribault, 1906; Murray, 1907) described complete eradiation of working groups. Much improvement in dust control has taken place in the industry since the turn of the century, but even recently those exposed in extremely dusty environments, such as textile mills, may have as much as 40% of their deaths attributable to this cause (Nicholson, 1976a). Groups with lesser exposures for 20 or more years, such as in mining and milling (Nicholson, 1976b) or insulation work (Selikoff et al., 1979) may have from 5% to 20% of their deaths from pneumoconiosis. All varieties of asbestos appear equally capable of producing asbestosis (Irwig et al. 1979). In groups exposed at lower concentrations, such as the families of workers, there is less incapacitation, and death from asbestosis has not been reported.

3.12 Manifestations of other occupational exposure to asbestos

In the past decade, considerable evidence has been developed on the prevalence of asbestos disease in workers exposed to a variety of work activities. Shipyard trades (other than insulation work), particularly, were shown to have had significant exposure. By 1975, Harries (1976) had identified 55 mesotheliomas in the Devonport Dockyard, only two of which were in asbestos workers. In a case-control study of four Atlantic Coast areas, an average relative risk for lung cancer of 1.4 was determined (Blot et al. 1978). The study population had an average employment time of only three years. However, no exposure data are available. X-ray abnormalities among non-insulator shipyard employees are also common. Among long-term (mostly 30+ year) shipyard workers, 86% were found to have X-ray abnormalities characteristic of asbestos exposure (Selikoff et al. 1980). Maintanance personnel have also been shown to be at risk from asbestos disease. Lilis et al. (1979) reported the finding of X-ray abnormalities among 55% of X-ray abnormalities of 20+ year chemical plant workers.

These findings are of importance because they point to sources of asbestos emission to the environment in the future. The removal of asbestos from friable products, including insulation material, and the installation of engineering controls in factories, have significantly reduced the exposure and emissions from primary manufacturing or primary using sources. However, over one million tons of asbestos is in place in friable materials in ships, building, power plants, chemical plants, refineries, and other locations of high temperature equipment (Nicholson, 1976a). The maintenance, repair and removal of this material will account for the principal exposures to workers and emissions into the environment (both in and out of buildings) in the future.

3.13 Deposition and clearance

Some limited data are available on the quantity of asbestos fibers in lungs of individuals with and without known exposures to asbestos (Sebastien et al., 1979; Jones et al., 1980; Wagner et al., 1982). Most of the cases analyzed were selected because of death from mesothelioma, often coupled with an investigation of a specific work group (Wagner et al., 1982; Berry and Newhouse, 1983). However, they have not been correlated with known cumulative exposures. Generally, amphibole burdens of individuals heavily exposed range from 10^7 to 19^8 fibers/gram dry weight; general population controls (in Great Britain) are usually less than 10^6 fibers/gram dry weight (Jones et al., 1980). Similar concentrations of chrysotile are seen in exposed workers (Wagner et al., 1982) and unexposed controls (Jones et al., 1980).

Very few data are available that provide a basis for establishing a model for the deposition and clearance of fibers in humans. It would be expected that both short- and long-term clearance mechanisms would exist in humans as in animals (See Chapter 4). If only long-term processes are considered (characterized by months or years) the simplest model is one in which the change in lung burden (N) is proportional to the rate of deposition of fibers (A) (assuming continuous exposure) diminished by a clearance that is proportional to (by factor β) to the number of fibers present.

$$\frac{dN}{dt} = A - \beta N$$

This yields for the number of fibers present after a constant exposure of duration, t_1,

$$N = \frac{A}{\beta}(1-e^{-\beta t_1})$$

and at a time, t_2 after cessation of a constant exposure of duration t_1

$$N = \frac{A}{\beta}(1-e^{-\beta t_1})e^{-\beta t_2}$$

Such a model would be applicable at times t_1 and t_2 which are long compared to any short-term clearance mechanisms. It is clearly a very simplistic model in that it considers only one characteristic time for long-term removal processes. Nevertheless, it illustrates the difficulty of applying even the simplest model. In order to systematize lung burdens, one needs information on the duration and intensity of the exposure and the time from last exposure in order to obtain a measure of the characteristic removal time for a given fiber type. Such information is not yet available for the individuals whose lungs have been analyzed.

Data have been presented by Bignon et al. (1978) on the number of amphibole fibers detected in lung washings of seven asbestos insulation workers. All were exposed between 10 and 16 years. While individual exposures were unknown, fewer fibers were found in the washings of those longest removed from exposure. The data are consistent with a decrease of 50% in the number of washable fibers at five to seven years after cessation of exposure. However, it should be noted that washable fibers may not be proportional to the residual lung burden, or to the number of fibers trapped within lung tissue. The lung washings were largely amphibole; no corresponding data are available for chrysotile fibers.

Data on the fiber dimensionality from these studies show a decrease in the average length and diameter of fibers found in the pleura compared with those found in the parenchyma. However, no distinction was made between amphiboles and chrysotile in this analysis and the different length-width data could simply be a reflection of the predominance of chrysotile in the pleura.

3.13.1 Models of deposition and clearance

The Task Group on Lung Dynamics of the International Commission on Radiological Protection has proposed a model for the deposition and retention of particles (See Brain and Valberg, 1974). The results of this model are shown in Figure 3-11 which depicts the percentages of particles of different sizes deposited in the various compartments of the respiratory tract. As can be seen, alveolar deposition is dominant for particles with a mass median diameter of less than 0.1 μm. As the particle size increases, deposition in this area decreases, falling to 25% at 1 μm and to 0 at 10 μm or above. Nasal and pharyngeal surface deposition becomes important above 1 μm and rises rapidly to be the dominant deposition site for particles 10 μm in diameter or greater. The above model was developed for spherical particles. Timbrell (1965) has shown that the settling velocities of particles and their aerodynamics are such that fibers with aspect ratios greater than three behave like particles with a diameter three times as great, independent of the length of the fiber. This has been corroborated by calculations of Harris and Fraser (1976). Thus, few fibers with diameters as large as 2 μm are likely to penetrate into the alveolar spaces, although finer fibers, even as long as 200 μm, may do so.

3.14 Effects of intermittent versus continuous exposures

Two distinct kinds of exposure occurred to workers in the different studies reviewed above. On the one hand, in some production operations (textiles, e.g.) workers would be exposed to a relatively con-

Figure 3-11

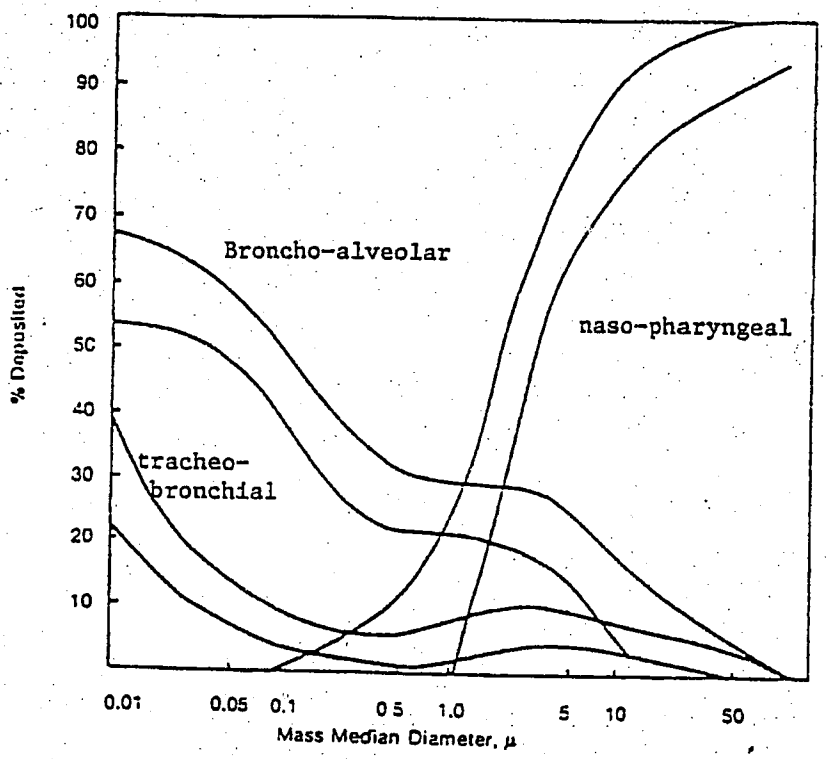

Fig. 3-11 Aerosol deposition in respiratory tract. Tidal volume is 1,450 ml; frequency, 15 breaths per minute. Variablilty introduced by change of sigma, geometric standard deviation, from 1.2 to 4.5. Particle size equals diameter of mass median size. (From: Brain and Valberg, 1974)

stant concentration of asbestos fiber throughout their work day. On the other hand, insulators, maintenance mechanics and some production workers are exposed to extremely variable concentrations of asbestos, with most of their cumulative exposure being the result of short duration, but intense, exposures. Implicit in the use of a linear dose-response relationship and average exposures is the concept that the risk of cancer is directly related to the cumulative asbestos exposure received in a period of time, i.e., the effect of an exposure to 100 f/ml for 1 hour is the same as that of 1 f/ml for 100 hours. (This equivalence applies only for short time periods. Because of the time dependence of mesothelioma risk, 100 f/ml for one year is not equivalent to 2 f/ml for 50 years.) Short, intense exposures could have an effect different from longer and lower exposure if clearance mechanisms are altered by very high concentrations of inspired asbestos. There are no data that directly address this question. However, indirect information suggests that the magnitude of the effect is less than the variability between studies with continuous exposure. Firstly, Henderson and Enterline (1979) found that the excess lung cancer risk for plant wide maintenance mechanics was only slightly higher (21%) than production workers on a unit exposure basis. Curiously, the risk of pneumoconiosis was much less per unit cumulative exposure among maintenance workers. Secondly, the similarity of unit exposure risks of insulators compared to groups with continuous exposure would suggest that the character of their exposure is not important. However, both comparisons depend upon the exposure estimates of the groups in question. Clearly, average exposures are difficult to estimate from episodic exposures and the above numerical similarities may be fortuitous. The unusually low pneumoconiosis risk among the mechanics in the Henderson and Enterline study may be the results of exposure misestimates.

3.15 Relative carcinogenicity of different asbestos varieties

Limited information exists on the effect of specific asbestos varieties in different exposure circumstances. Considerable controversy has developed as to whether one variety of asbestos (crocidolite) or

mineral class (amphibole) is more carcinogenic than another (the serpentine mineral, chrysotile). Both Great Britain and Sweden have imposed far more rigid standards for crocidolite than other varieties of asbestos. In contrast, the United States has no special standard for any specific asbestos mineral.

A special role has been attributed to crocidolite by some investigators, perhaps because the first environmental mesotheliomas were found in an area where crocidolite exposure was likely (Wagner et al. 1960). Subsequently, in Great Britain, where crocidolite was often used, many individuals developing mesotheliomas could be found to have had opportunities for exposure to this fiber, although such association was not unique. In fact, equal opportunity for exposure for chrysotile was demonstrated (Greenberg and Lloyd Davies, 1974). While crocidolite is a factor in an increased risk of death from mesothelioma in some circumstances, in others this cannot be demonstrated. Considerable data indicate that significant risks of mesothelioma exist in particular circumstances from exposure to other asbestos varieties.

Enterline and Henderson (1973) and Weill et al. (1979) suggested that workers exposed to chrysotile and crocidolite may have had a greater lung cancer risk than those exposed to chrysolite alone. These suggestions were based on air concentrations of total particles in the respective work environments (and included much other dust as cement). A significantly added crocidolite exposure could have been present in the combined exposure work circumstances without significantly affecting the total particle count.

The manufacture of amosite insulation has been shown to be associated with a high risk of mesothelioma (See Table 3-11), while amosite mining has demonstrated little excess risk of death from mesothelioma (Webster, 1970). Similarly, data on chrysotile use is ambiguous. Exposures in the British factory studied by Peto (1980), which predominently used chrysotile carried a high risk of mesothelioma but recently questions were raised over the use of some crocidolite in the

facility. No data are available on the relative amounts used of each fiber. Over 4% (4.3%) of the deaths were from mesothelioma in a long-term follow-up of a facility that used 5000-6000 tons of chrysotile, 50 tons of amosite and 4 tons of crocidolite annually (except for three years when 375 tons of amosite were used) (Robinson et al. 1978). In contrast, only one mesothelioma occurred in 175 deaths in the factory studied by Dement et al. (1982).

Much of these differences in risk may be accounted for by the differences in fiber size distributions in the three work environments rather than fiber type. The greatest percentage of longer and thicker fibers would occur in the work environment of miners and millers. When asbestos is used in manufacturing processes, it is broken apart as it is incorporated in finished products. During application or removal of insulation products, it is further manipulated and the fibers become reduced in length and diameter. As these smaller fibers can readily be carried to the periphery of the lung, penetrate the visceral pleura and lodge in the visceral or parietal pleura, they may be of importance in the etiology of mesothelioma. Bignon, Sebastien, and their colleagues (1978) have reported data from a study of lungs and pleura of shipyard workers. Larger fibers, often amphibole tended to be found in lung tissue. In the pleura, the fibers were generally chrysotile, but finer and smaller. The early association of mesothelioma with crocidolite occurred because, even in mining, it is readily broken apart and its extensive use in Great Britain in extremely dusty circumstances (spray insulation e.g.) created high exposures for many individuals with a concomitant high risk of death from mesothelioma. The mining and milling of chrysotile, on the other hand, involved exposure to long and curly fibers which are easily counted, but not easily inspired.

Recent exposure to the fibrous zeolite mineral, erionite, in Turkey has been associated with mesothelioma. Results reported by Baris et al. (1979) demonstrate an extraordinary risk. Annual incidence rates for mesothelioma of nearly 1% exist. In 1974, 11 of 18 deaths in Karain, Turkey were from this cause. Seventy-five percent of the

fiber diameters are reported to be less than 0.25 μm. The lengths were highly variable but most fibers were shorter than 5 μm. Asbestos minerals in identified geological deposits are not reported to occur in the area.

3.16 Summary

Data are available that allow unit risk to be made for lung cancer and allow such risks to be made for mesothelioma. The values for K_L, the fractional risk per f-y/ml, vary widely among the studies, largely because of the statistical variability associated with numbers but also because of uncertainties associated with methodology and exposure estimates. However, because of this variability, the range of possible unit risks from all studies but one lies within a range of K_L from 0.003 to 0.03. Similar data obtained for K_M the potency coefficient for mesothelioma risk. Its value would appear to lie between 3×10^{-9} and 3×10^{-8}. Differences in asbestos type cannot explain the variation. However, lower risk values found in chrysotile mining would suggest that fiber dimensionality is important.

4. ANIMAL STUDIES

4.1 Introduction

Animal studies of asbestos health effects largely have been confirmatory of previously established human data rather than serving as predictors of human disease. This has occurred in part because, 1) asbestos usage predated the use of animal studies for ascertainment of risk, 2) the animal models utilized were relatively resistant to the human diseases that are of concern, 3) the principal carcinogenic risk from asbestos, lung cancer, is the result of a multifactorial interaction between other agents, principally cigarette smoking, and asbestos exposure and is difficult to elicit in a single exposure circumstance. All of the asbestos-related malignancies were first identified in humans. Nevertheless, the experimental studies have confirmed the identification of disease and provided important information not available from human studies on the deposition, clearance and retention of fibers, as well as on cellular changes at short times after exposure. Unfortunately, one of the most important questions raised by human studies, that of the role of fiber type and size, is only partially answered by animal research. Injection and implantation studies have shown longer and thinner fibers to be more carcinogenic once in place at a potential site of cancer. However, the size dependence of the movement of fibers to mesothelial and other tissues is not full elucidated and the questions raised in the human studies concerning the relative carcinogenicity of different asbestos varieties still remains.

4.2 Fiber deposition and clearance

The deposition and clearance of fibers from the respiratory tract of rats has been studied directly by Morgan and his colleagues (Morgan et al. 1975; Evans et al. 1973) using radioactive asbestos samples. Following 30 minute inhalation exposures in a nose breathing apparatus, the deposition and clearance from the respiratory tract were followed. At the conclusion of the inhalation, the distribution in various organ

systems was determined. Thirty-one percent to 68% of the inspired fibrous material was deposited in the respiratory tract. The distributions of that deposited are shown in Table 4-1. Rapid clearance, largely from the upper respiratory tract (airways above the trachea), occurred within 30 minutes with up to two-thirds of the fibers being swallowed and found in the gastrointestinal tract.

Clearance from the lower respiratory tract (trachea to alveoli) proceeds slower with two distinct components being observed. The first, believed to be due to macrophage movement leads to the elimination of a considerable portion of the material deposited in the lower respiratory tract with a half life of six to ten hours. A slower phase with a half life of sixty to eighty days follows which involves the clearance from alveolar spaces. Data for a synthetic fluoramphibole are depicted in Figure 4-1, which show one short and two long-term components for the clearance of fibers. Other data on the lung content of animals sacrificed at various times after exposure show only a single long-term clearance component (Morgan et al., 1978). An anomaly seen, however, is that the ratio of fibers in the feces to those in the lung at time of sacrifice is not a constant as would be expected from a single exponential clearance mechanism.

By extrapolating curves like that of Figure 4-1 to zero-time for a variety of fibers, it is possible to ascertain the relative amounts deposited in the bronchiolar-alveolar spaces. These data are shown for different fibers in Figure 4-2, along with estimates of the percentage of material deposited in the upper respiratory tract. The relative similarity of the percentage deposited in the lower bronchioles or alveoli for different fiber diameters is a reflection of two competing processes. At lower fiber diameters, fibers can be inspired and then expired without impaction in the lower respiratory tract. As the fiber diameter increases, impaction in the upper respiratory tract becomes important, which leads to a lower percentage being carried to the alveolar spaces.

TABLE 4-1

Distribution of Fiber at the Termination of 30 minute exposures
(% of Total Deposited)

Fiber	Nasal Passages [a]	Esophagus	GI Tract	Lower Respiratory Tract	Percent deposited[b]
Chrysotile A	9 ± 3	2 ± 1	51 ± 9	38 ± 8	31 ± 6
Chrysotile B	8 ± 2	2 ± 1	54 ± 5	36 ± 4	43 ± 14
Amosite	6 ± 1	2 ± 1	57 ± 4	35 ± 5	42 ± 14
Crocidolite	8 ± 3	2 ± 1	51 ± 9	39 ± 5	41 ± 11
Anthophyllite	7 ± 2	2 ± 1	61 ± 8	30 ± 8	64 ± 24
Fluoramphibole	3 ± 2	1 ± 1	67 ± 5	29 ± 4	68 ± 17

From: Morgan, et al. (1975)

[a] Mean and SD

[b] (of total inspired)

Figure 4-1

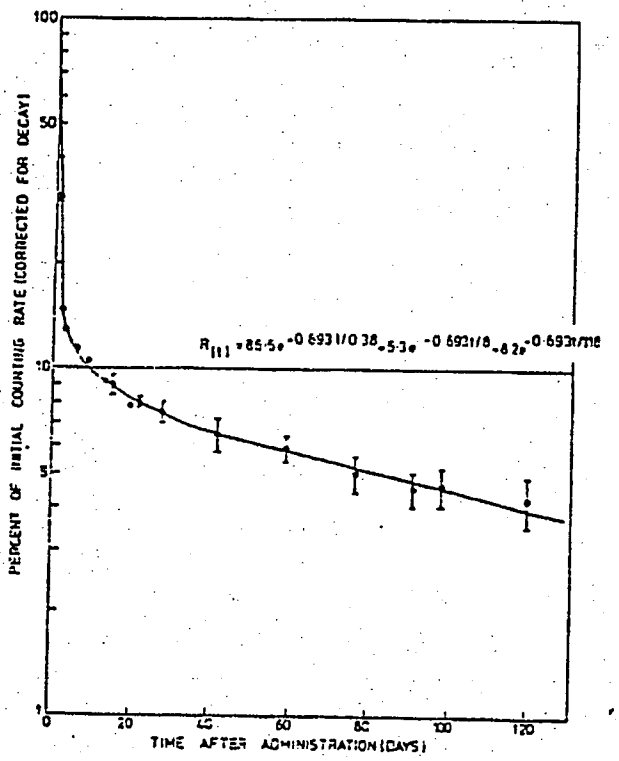

Fig. 4-1 Measurements of animal radioactivity (corrected for decay) at various times after inhalation exposure to synthetic flouramphibole. Mean result for three animals expressed as a percentage of the counting rate measured immediately after exposure. From: Morgan et al. (1977)

Figure 4-2

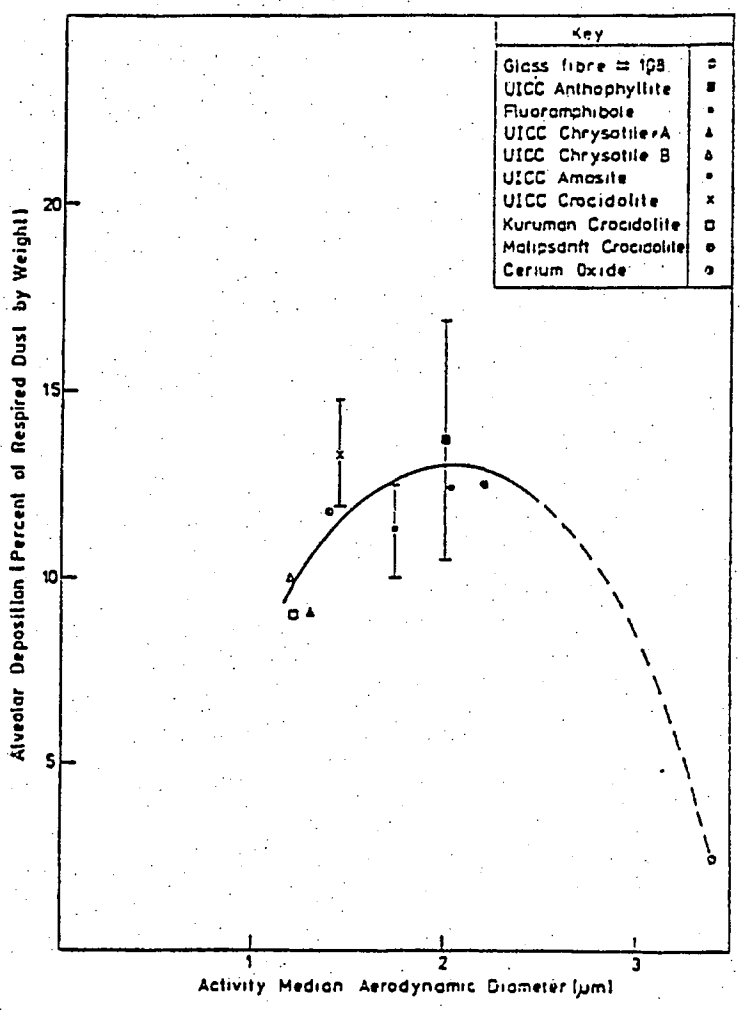

Fig. 4-2 Correlation between the alveolar deposition of a range of fibrous and non-fibrous particles inhaled by the rat, and the corresponding activity median aerodynamic diameters.
From: Morgan (1979)

Morgan et al. (1978) have also studied the length distribution of fibers remaining in the lungs of rats in order to determine the significance of fiber length on clearance. He found that the shorter fibers are preferentially removed during the first week after inhalation. The fibers recovered within this first week in bronchial washings show few fibers longer than 15 μm in length and very few exceeding 20 μm, which suggest that fibers of such sizes are trapped within the alveolar spaces.

The radioactive chrysotile used in the clearance experiments allow autoradiography to demonstrate the location of fibers at different times after exposure. At 48 hours after exposure, the distribution of fibers in the lung was relatively uniform. However, at later times, there was a movement of fibers to the periphery of the lung where they accumulated in subpleural foci consisting of alveoli filled with fiber-contained cells.

Other data on the deposition and retention of inhaled asbestos have been reported by Wagner et al. (1974). Figure 4-3 shows the dust content of rat lungs following exposures to different asbestos varieties. In the case of amphibole exposures, a linear increase in the amount of retained fiber was seen, whereas for chrysotile the content of the lung rapidly reached an equilibrium between removal or dissolution processes and deposition and did not increase thereafter. The long-term build-up of the amphiboles indicates that in addition to the clearance processes observed by Morgan, Holmes and Evans that there is a virtual permanent retention of some fibers. Using a minute volume for the rat of 100 ml, it would appear that about one percent of the total crocidolite or amosite inhaled is permanently in the lung.

The finding of a rapid movement from the upper respiratory tract and a slower clearance from the lower respiratory tract to the gastrointestinal tract demonstrates a route of exposure that may be important for gastrointestinal cancer. The observation in humans of peritoneal mesothelioma, excess cancer of the stomach, colon, and rectum, and

Figure 4-3

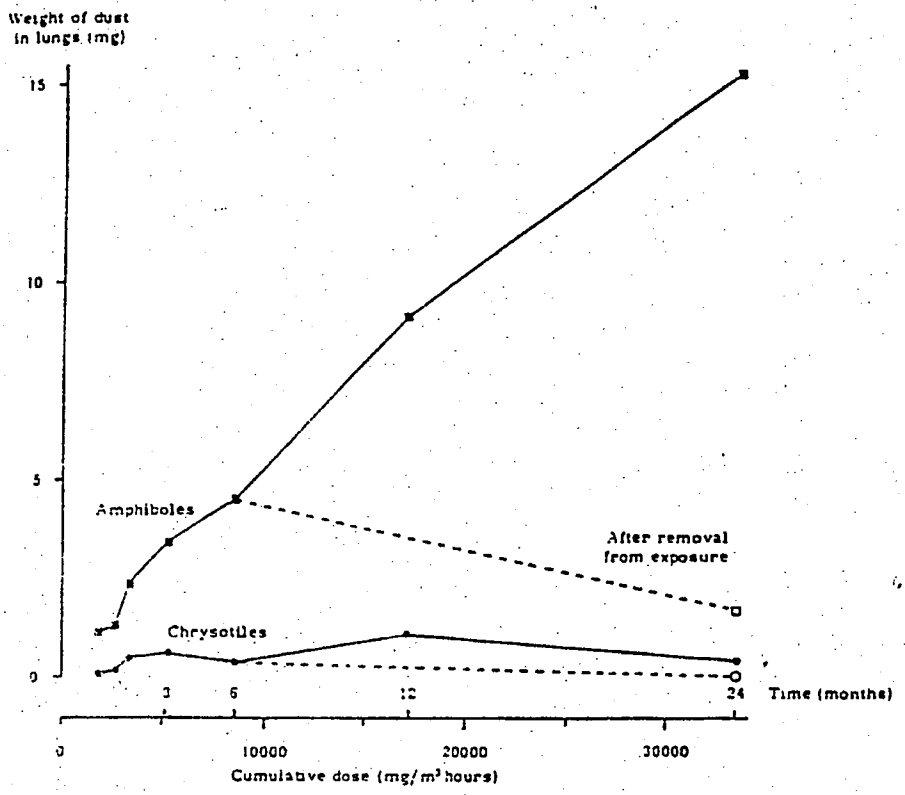

Fig. 4-3 Mean weight of dust in lungs of rats in relation to dose and time. From: Wagner et al. (1974)

possibly cancers at other non-respiratory sites, such as the kidney could result from the migration of such fibers to and across the gastrointestinal mucosa. Additionally, fibers may reach organs in the peritoneal cavity by transdiaphragmatic migration or lymphatic-hematogenous transport.

4.3 Cellular alterations

Several studies describe cellular changes in animals following exposure to asbestos. Holt et al. (1964) described early (14-day) local inflammatory lesions found in the terminal bronchioles of rats following inhalation of asbestos fibers. These consisted of multinucleated giant cells, lymphocytes and fibroblasts. Progressive fibrosis followed within a few weeks of the first exposure to dust. Davis, et al. (1978) described similar early lesions in rats consisting of a proliferation of macrophages and cell debris in the terminal bronchioles and alveolae.

Jacobs et al. (1978) fed rats 0.5 mg or 50 mg of chrysotile daily for 1 week or 14 months and subsequently examined gastrointestinal tract tissue by light and electron microscopy. No effects were noted in esophagus, stomach or cecum tissue but structural changes in the ileum were seen, particularly of the villi. Considerable cellular debris was present by light microscopy in the ileum, colon, and rectum tissue. The electron microscopic data confirmed that of light microscopy and indicated the observed changes were consistent with a mineral-induced cytotoxicity.

A single oral administration of from 5 to 100 mg/kg of chrysotile to rats has produced a subsequent increase in thymidine in the stomach, duodenum, and jejunum (Amacher, et al. 1975). This suggests that an immediate response of cellular proliferation and DNA synthesis may be stimulated by chrysotile ingestion.

4.4 Mutagenicity

Asbestos has not been shown to be mutagenic in Escherichia coli or Salmonella typhimurium tester strains (Chamberlain and Tarmy, 1977). Newman et al. (1980) reported that asbestos has no mutagenic ability in Syrian hamster embryo cells, but may increase cell permeability and allow other mutagens into the cell. However, Sincock (1977) using several chrysotile, amosite and crocidolite samples, showed that an increased frequency of polyploids and cells with fragments resulted from passive inclusion of asbestos in the culture media of CHO-K1 Chinese hamster cells. Similarly, Lavappa et al. (1975) showed that chrysotile induced a significant and exposure-related increase in chromosome aberrations in cultured Syrian hamster embryo cells. Amosite, chrysotile and crocidolite have been found to be weakly mutagenic in Chinese hamster lung cells in the 6-thioguanine-resistance assay (Huang, 1979). Finally, Livingston et al. (1980) have shown that exposure to crocidolite and amosite can increase the sister chromatid exchange rate in Chinese hamster ovarian fibroblasts.

4.5 Inhalation studies

The first unequivocal data showing a relationship between asbestos inhalation and lung malignancy in laboratory animals was that of Gross, et al. (1967) who observed carcinomas in rats exposed to a mean concentration of 86 mg/m^3 chrysotile for 30 hours/week from the age of six weeks. Of 72 rats surviving for 16 months or longer, 19 developed adenocarcinomas, 4 developed squamous cell carcinomas, and 1, a mesothelioma. No malignant tumors were found in 39 control animals. A search was made for primaries at other sites which could have metastasized. None were found. These and other data are summarized in Table 4-2.

Reeves et al. (1971) found 2 squamous cell carcinomas in 31 rats sacrificed after 2 years following exposure to about 48 mg/m^3 of

TABLE 4-2

Summary of Experiments on the Effects of Inhalation of Asbestos

Animal Species	Material Administered	Dosage	Animals Examined for Tumors	Findings (malignant tumors)	Average Survival Time
		Gross, et al. (1967)			
132 male white rats	ball-and-hammer-milled Canadian chrysotile with/without 0.05 ml intratracheal 5 percent NaOH	42-146 mg/m³ (mean conc., 86 mg/m³) for 30 hrs/week	72	17 adenocarcinomas 4 squamous-cell sarcomas 7 fibrosarcomas 1 mesothelioma	not available
55 male white rats	controls with/without 5 percent NaOH	control	39	none	not available
		Reeves, et al. (1971)			
206 rats 106 rabbits 139 guinea pigs 214 hamsters	ball-milled chrysotile, amosite, and crocidolite	48±2 mg/m³ for 16 hrs/week up to 2 yrs	not available	2 squamous-cell carcinomas in 31 animals from crocidolite exposure	no information periodic sacrifices were made
		Reeves, et al. (1974)			
219 rats 216 gerbils 100 mice 72 rabbits 100 guinea pigs	ball-and- hammer-milled chrysotile, amosite, and crocidolite	48±2 mg/m³ for 16 hrs/week up to 2 yrs	120 rats 116 gerbils 10 mice 30 rabbits 43 guinea pigs	10 malignant tumors in rats 2 in mice (Table 4-3)	no information periodic sacrifices were made

TABLE 4-2 (continued)

Summary of Experiments on the Effects of Inhalation of Asbestos

Animal Species	Material Administered	Dosage	Animals Examined for Tumors	Findings (malignant tumors)	Average Survival Time
			Wagner, et al. (1974)		
13 groups of approx. 50 and 15 of about 25 Wistar SPF rats	amosite anthophyllite crocidolite Canadian chrysotile Rhodesian chrysotile (UICC samples)	10.1 to 14.7 mg/m^3 for 1 day to 24 months, 35 hrs/week	849	(See Tables 4-4 and 4-5) All asbestos varieties produced mesothelioma and lung cancer, some from exposure as short as 1 day	669 to 857 days versus 754 to 801 for controls. Survival times not significantly affected by exposure.
			Wagner, et al. (1977a)		
CD Wistar male and female rats	superfine chrysotile	10.8 mg/m^3 37.5 hrs/wk for 3, 6, or 12 months		1 adenocarcinoma of the lung in 24 animals exposed for 12 months	
CD Wistar male and female rats	nonfibrous cosmetic talc			none	
			Davis, et al. (1978)		
46 groups of approx. 11an SPF rats and 20 11an SPF rats	UICC samples of amosite chrysotile crocidolite	2 mg/m^3 and 10 mg/m^3 35 hours/wk for 224 days	208	7 adenocarcinomas 3 squamous-cell sarcomas 1 pleural mesothelioma 1 peritoneal mesothelioma	not available sacrificed at 29 months
20 11an SPF rats	control	control	20	none	

crocidolite. No malignant tumors were reported in rabbits, guinea pigs, hamsters, or in animals exposed to similar concentrations of chrysotile or amosite. No details of the pathological examinations were given.

In a later study (Reeves et al. 1974), malignant tumors developed in 5 to 14 percent of the rats surviving 18 months. Lung cancer and mesothelioma were produced by exposures to amosite and chrysotile and lung cancer by crocidolite inhalation. Again, significant experimental details were lacking; information on survival times and times of sacrifice would have been useful. Available details of the exposures and results are given in Table 4-3. While the relative carcinogenicity of the fiber types was similar, it was noted that the fibrogenic potential of chrysotile, which had been substantially reduced in length and possibly altered (Langer, et al. 1978) by milling was much less than that of the amphiboles. These results were also discussed in a later paper by Reeves (1976).

The most important series of animal inhalation studies is that of Wagner et al. (1974, 1977b). He exposed 849 Wistar SPF rats to the five UICC (Union Intranationale Contra le Cancer) asbestos samples at concentrations from 10.1 to 14.7 mg/m^3 for times ranging from 1 day to 24 months. These concentrations are typically 10 times those measured in dusty asbestos workplaces during earlier decades. For all exposure times, there were 50 adenocarcinomas, 40 squamous-cell carcinomas, and 11 mesotheliomas produced. All varieties of asbestos produced mesothelioma and lung malignancies, in some cases from exposures as short as one day. Data from these experiments are presented in Tables 4-4 and 4-5. These tumors follow a reasonably good linear relationship for exposure times of 3 months or greater. The incidence in the 1-day exposure group, however, is considerably greater than expected. It was noted that exposure had a limited effect on length of life. Average survival times varied from 669 to 857 days for exposed animals versus 754 to 803 days for controls. The development of asbestosis was also documented. There were 17 lung tumors, 6 in animals with no evidence of asbestosis and 11 in rats with minimal or slight asbesto-

TABLE 4-3

Experimental Inhalation Carcinogenesis

Fiber	Exposure[a] Mass (mg/m³)	Exposure[a] Fiber (f/ml)	Rats Animals Examined	Rats Malignant Tumors	Mice Animals Examined	Mice Malignant Tumors
Chrysotile	47.9	54	43	1 lung papillary carcinoma 1 lung squamous-cell carcinoma 1 pleural mesothelioma	19	none
Amosite	48.6	864	46	2 pleural mesotheliomas	17	none
Crocidolite	50.2	1,105	46	3 squamous-cell carcinomas 1 adenocarcinoma 1 papillary carcinoma - all of the lung	18	2 papillary carcinomas of bronchus
Controls			5	none	6	1 papillary carcinoma of bronchus

From: Reeves, et al. (1974)

[a] The asbestos was comminuted by vigorous milling, after which 0.00% to 1.02% of the airborne mass was of fibrous morphology (3:1 aspect ratio) by light microscopy.

TABLE 4-4

Number of Rats with Lung Tumors or Mesotheliomas After Exposure to Various Forms of Asbestos Through Inhalation

Form of Asbestos	No. of Animals	Adenocarcinomas	Squamous-cell Carcinomas	Mesothelioma
Amosite	146	5	6	1
Anthophyllite	145	8	8	2
Crocidolite	141	7	9	4
Chrysotile (Canadian)	137	11	6	4
Chrysotile (Rhodesian)	144	19	11	0
None	126	0	0	0

From: Wagner, et al.(1974)

TABLE 4-5

Numbers of Rats with Lung Tumors or Mesotheliomas After Various Lengths of Exposure to Various Forms of Asbestos Through Inhalation

Length of Exposure	No. of Animals	No. with Lung Carcinomas	No. with Pleural Mesotheliomas	% of Animals with Tumors
None	126	0	0	0.0
1 day	219	3[a]	2[b]	2.3
3 months	180	8	1	5.0
6 months	90	7	0	7.8
12 months	129	35	6	31.8
24 months	95	37	2	41.0

From: Wagner et al. (1974)

2 exposed to chrysotile and 1 to crocidolite

1 exposed to amosite and one to crocidolite

sis. Cancers at extrapulmonary sites were also listed. Seven malignancies of ovary and 8 of male genitourinary organs were observed in the exposed groups of approximately 350 male and female rats. None were observed in control groups of 60 males and females. Incidence of malignancy at other sites was little different from that of controls. However, the authors note that if controls are included from other experiments in which ovarian and genitourinary tumors were present, the comparative incidence in the exposed groups here lacks statistical significance. No data were provided, however, on the variation of tumor incidence at extrapulmonary sites with asbestos dosage.

Wagner et al. (1977a) also compared effects of inhalation of a superfine chrysotile to a pure nonfibrous talc. One adenocarcinoma was found in 24 rats exposed to 10.8 mg/m^3 of chrysotile for 37.5 hours/week for 12 months.

In a study similar to Wagner's, Davis et al. (1978) exposed rats to 2.0 or 10.0 mg/m^3 of chrysotile, crocidolite, and amosite (equivalent to from 430 to 1950 f/ml). Adeno- and squamous cell carcinomas were observed in chrysotile exposures, but not with crocidolite or amosite (see Table 4-6). One pleural mesothelioma was observed with crocidolite exposure, and extrapulmonary neoplasms included a peritoneal mesothelioma. A relatively large number of peritoneal connective tissue malgnancies were also observed, including a leimyofibroma on the wall of the small intestine. The meaning of these tumors is not clear.

Inhalation exposures result in concomitant gastrointestinal exposures from the asbestos that is swallowed after clearance from the bronchial tree. While all inhalation experiments focus on thoracic tumors, those of Wagner et al. (1974), Davis et al. (1978) and, to a limited extent, Gross et al. (1967) also included a search for tumors at extrathoracic sites. A limited number of these were found, but no association can be made with asbestos exposure.

One aspect of the inhalation experiments that is noteworthy is the number of pulmonary neoplasms that can be produced in the rat by

TABLE 4-6

Experimental Inhalation Carcinogenesis in Rats

	Exposure		Number of Animals Examined	Malignant Tumors
	Mass (mg/m^3)	Fiber ($f>5u/ml$)		
Chrysotile	10	1,950	40	6 adenocarcinomas 2 squamous-cell carcinomas
Chrysotile	2	390	42	1 squamous-cell carcinoma 1 peritoneal mesothelioma
Amosite	10	550	43	none
Crocidolite	10	860	40	none
Crocidolite	5	430	43	1 pleural mesothelioma
Control			20	none

From: Davis et al. (1978)

inhalation as compared to other species (Reeves et al. 1971, 1974). This points to the variability of species response to asbestos and the need for an appropriate model before extrapolations to man can be made with confidence. The absence of significant gastrointestinal malignancy from asbestos exposure in animals, in contrast to that found in humans, may be the result of the use of inappropriate animal models.

4.6 Intrapleural administration

Evidence that intrapleural administration of asbestos would result in mesothelioma was forthcoming in 1970 when Donna (1970) produced mesotheliomas in Sprague-Dawley rats treated with a single dose of 67 mg of chrysotile, amosite, or crocidolite. Reeves et al. (1971) produced mesothelial tumors in rats (1 of 3 with crocidolite and 2 of 12 with chrysotile by intrapleural injection of 10 mg of asbestos. Two of 13 rabbits injected with 16 mg of crocidolite developed mesotheliomas.

Stanton and Wrench (1972), in a series of experiments, demonstrated that major commercial varieties of asbestos, as well as various other fibers, produced mesotheliomas in as many as 75 percent of animals into which material had been surgically implanted onto the pleural surface. The authors concluded that the carcinogenicity of asbestos and other fibers is strongly related to their physical size, those fibers of a diameter less than 3 μm being carcinogenic and those of a larger diameter not carcinogenic. Further, samples treated by grinding in a ball mill to produce shorter length fibers were less likely to produce tumors. While the authors attributed the reduced carcinogenicity to a shorter fiber length, the question has been raised as to the effect of the destruction of crystallinity and perhaps other changes in the fibers occasioned by the extensive ball milling (Langer et al. 1978).

Since 1972, Stanton and his coworkers (Stanton et al., 1977; 1981) have continued these investigations of the carcinogenic action of durable fibers. Table 4-7 summarizes the results of 72 different experiments. In their analyses Stanton et al. (1981) suggest that the

Table 4-7

Summary of 72 experiments with different fibrous materials

Expt No.	Compound	Actual tumor incidence	Percent tumor probability ± SD	Common log fibers/μg, ≤0.25 μm × >8 μm	Expt No.	Compound	Actual tumor incidence	Percent tumor probability ± SD	Common log fibers/μg, ≤0.25 μm × >8 μm
1	Titanate 1	21/29	95±4.7	4.94	37	Halloy 1	4/25	20±9.0	0
2	Titanate 2	20/29	100	4.70	38	Halloy 2	5/28	23±9.3	0
3	Si carbide	17/26	100	5.15	39	Glass 8	3/26	19±10.3	3.01
4	Dawson 5	26/29	100	4.94	40	Crocid 11	4/29	19±8.5	0
5	Tremolite 1	22/28	100	3.14	41	Glass 19	2/28	15±9.0	0
6	Tremolite 2	21/28	100	2.84	42	Glass 9	2/28	14±9.4	1.84
7	Dawson 1	20/25	95±4.8	4.66	43	Alumin 6	2/28	13±8.8	0.82
8	Crocid 1	18/27	94±6.0	5.21	44	Dawson 6	3/30	13±6.9	0
9	Crocid 2	17/24	93±6.5	4.30	45	Dawson 2	2/27	12±7.9	0
10	Crocid 3	15/23	93±6.9	5.01	46	Wollaston 2	2/25	12±8.0	0
11	Amosite	14/25	93±7.1	3.53	47	Crocid 12	2/27	10±7.0	3.73
12	Crocid 4	15/24	86±9.0	5.13	48	Attapul 2	2/29	11±7.5	0
13	Glass 1	9/17	85±13.2	5.16	49	Glass 10	2/27	8±5.6	0
14	Crocid 5	14/29	78±10.8	3.29	50	Glass 11	1/27	8±5.5	0
15	Glass 2	12/31	77±16.6	4.29	51	Titanate 3	1/28	8±8.0	0
16	Glass 3	20/29	74±8.5	3.59	52	Attapul 1	2/29	8±5.3	0
17	Glass 4	18/29	71±9.1	4.02	53	Talc 1	1/26	7±6.9	0
18	Alumin 1	15/24	70±10.2	3.63	54	Glass 12	1/25	7±5.4	0
19	Glass 5	16/25	69±9.6	3.00	55	Glass 13	1/27	6±5.7	0
20	Dawson 7	16/30	68±9.3	4.71	56	Glass 14	1/25	6±5.5	0
21	Dawson 4	11/26	66±12.2	4.01	57	Glass 15	1/24	6±5.9	1.30
22	Dawson 3	9/24	56±13.4	5.73	58	Alumin 7	1/25	5±5.1	0
23	Glass 6	7/22	64±17.7	4.01	59	Glass 16	1/29	5±4.4	0
24	Crocid 6	9/27	63±13.9	4.60	60	Talc 3	1/29	4±4.3	0
25	Crocid 7	11/26	56±11.7	2.65	61	Talc 2	1/30	4±3.8	0
26	Crocid 8	8/25	53±12.9	0	62	Talc 4	1/29	5±4.9	0
27	Alumin 2	8/27	44±11.7	2.95	63	Alumin 8	1/28	3±3.4	0
28	Alumin 3	9/27	41±10.5	2.47	64	Glass 21	2/47	6±4.4	0
29	Crocid 9	8/27	33±9.8	4.25	65	Glass 22	1/45	2±2.3	0
30	Wollaston 1	5/20	31±12.5	0	66	Glass 17	0/28	0	0
31	Alumin 4	4/25	29±12.0	2.60	67	Glass 18	0/115	0	0
32	Crocid 10	6/29	37±13.5	3.09	68	Crocid 13	0/29	0	0
33	Alumin 5	4/22	22±9.3	3.73	69	Wollaston 4	0/24	0	0
34	Glass 20	4/25	22±10.0	0	70	Talc 5	0/30	0	0
35	Glass 7	5/28	21±8.7	2.50	71	Talc 6	0/30	0	3.30
36	Wollaston 3	3/21	19±10.5	0	72	Talc 7	0/29	0	0

From: Stanton et al. (1981)

best measure of carcinogenic potential is the number of fibers that measure $\leq$ 0.25 μm in diameter and $\geq$ 8 μm in length, although a good correlation of carcinogenicity is also obtained for fibers $\leq$ 1.5 μm in diameter and $\geq$ 4. μm in length. The logit distribution of tumor incidence against the log of the number of particles $\leq$ 0.25 μm x $\geq$ 8 μm is shown in Figure 4.4. The regression equation for the dotted line is:

$$\ln[p/(1-p)] = -2.62 + 0.93 \log x$$

where p is the tumor probability and x the number of particles < 0.25 μm x > 8 μm. A reasonable relationship with data exists, but substantial discrepancies occur, suggesting the possibility that other relationships may better fit the data. Bertrand and Pézerat (1980) have suggested that carcinogenicity may correlate as well with the ratio of length to width (aspect ratio).

Another comprehensive set of experiments was conducted by Wagner (Wagner et al. 1973, 1977b). He, too, produced mesothelioma from intrapleural administration of asbestos to CD Wistar rats and demonstrated a strong dose-response relationship. Tables 4-8 and 4-9 list the results of these experiments.

Pylev and Shabad (1973) and Shabad et al. (1974) reported mesotheliomas in 18 of 48 and in 31 of 67 rats injected with three doses of 20 mg of Russian chrysotile. Other experiments by Smith and Hubert (1974) have produced mesotheliomas in hamsters injected with 10 to 25 mg of chrysotile, 10 mg of amosite or anthophyllite, and 1 to 10 mg of crocidolite.

Various suggestions have been made that natural oils and waxes contaminating asbestos fibers might be related to their carcinogenicity (Harington, 1962; Harington and Roe, 1965; Commins and Gibbs, 1969). This, however, was not borne out in the experiments described above by Wagner et al. (1973) or Stanton and Wrench (1972).

4.7 Intratracheal injection

Intratracheal injection has been used to study the combined effect of

Figure 4-4

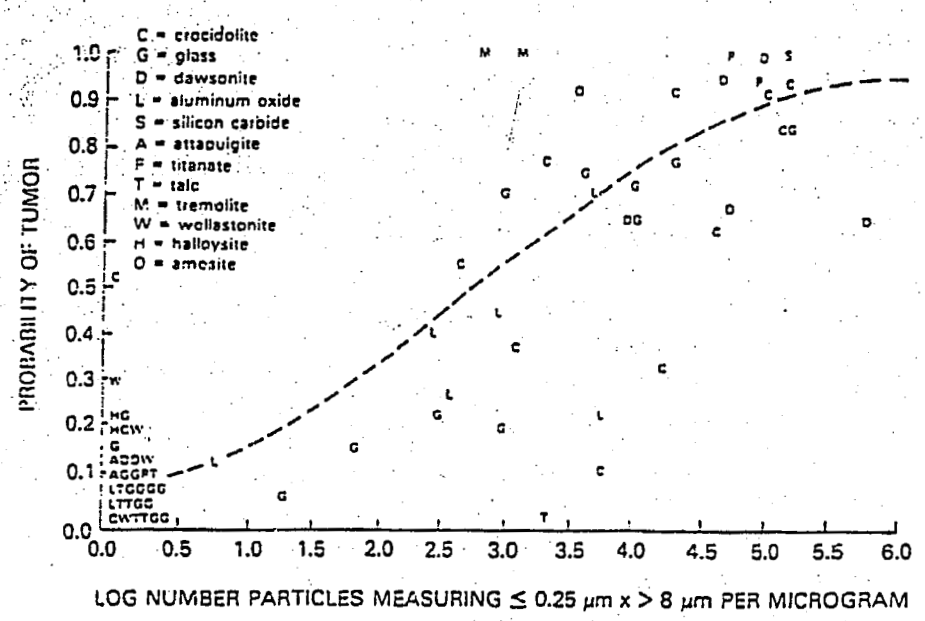

Fig. 4-4 Regression curve relating probability of tumor to logarithm of number of particles per μg with diameter ≤ 0.25 μm and length >8 μm. From: Stanton et al. (1981)

Table 4-8

Percentage of Rats Developing Mesotheliomas After Intrapleural Administration of Various Materials[a]

Material	Percent of Rats with Mesotheliomas
SFA chrysotile (superfine Canadian sample)	66
UICC crocidolite	61
UICC amosite	36
UICC anthophyllite	34
UICC chrysotile (Canadian)	30
UICC chrysotile (Rhodesian)	19
Fine glass fiber (code 100), median diameter, 0.12 μm	12
Ceramic fiber, diameter, 0.5-1 μm[b]	10
Glass powder	3
Coarse glass fiber (code 110), median diameter, 1.8 μm	0

[a] From Wagner et al. (1977b)

[b] From Wagner et al. (1973)

TABLE 4-9

Dose-Response Data Following Intrapleural Administration of Asbestos to Rats

Material	Dose (mg)	No. of Rats with Mesothelioma	Total no. of Rats	% of Rats with Tumors
SFA chrysotile	0.5	1	12	8
	1	3	11	27
	2	5	12	42
	4	4	12	33
	8	8	12	62
Crocidolite	0.5	1	11	9
	1	0	12	0
	2	3	12	25
	4	2	13	15
	8	5	11	45

From: Wagner et al. (1973)

administration of chrysotile with benz(a)pyrene in rats or hamsters. In rats given three doses of 2 mg chrysotile (Shabad et al. 1974) or hamsters given 12 mg of chrysotile (Smith et al. 1970) no lung tumors were observed. However, the coadministration of benzo(a)pyrene did result in lung tumors suggesting a cocarcinogenic or synergistic effect.

4.8 Intraperitoneal administration

Intraperitoneal injections of 20 mg of crocidolite or chrysotile produced three peritoneal mesotheliomas in 13 Charles River CD rats. Twenty mg of amosite produced no tumors in a group of 11 (Maltoni and Annoscia, 1974). They also injected 25 mg of crocidolite into 50 male and 50 female 17 week old Sprague-Dawley rats and observed 31 mesothelial tumors in males and 34 in females.

In an extensive series of experiments, Pott and Friedrichs (1972) and Pott et al. (1976) produced peritoneal mesotheliomas in mice and rats injected with various commercial varieties of asbestos and other fibrous material. These results are shown in Table 4-10. Using experiments with intrapleural administration, the malignant response was altered by ball-milling fibers for 4 hours. The rate of tumor production was reduced from 55 percent to 32 percent and the time from onset of exposure to first tumor was lengthened from 323 to 400 days following administration of four doses of 25 mg of UICC Rhodesian chrysotile. In the the case of the ball-milled fiber, 99% were reported to be smaller than 3 μm, 93 percent less than 1 μm, and 60 percent less than 0.3 μm.

Pott (1980) has proposed a model for the relative carcinogenicity of mineral fibers according to their dimensionality using the results of injection and implantation data. Figure 4-5 shows the schematic features of this model. Greatest carcinogenicity is attributed to fiber lengths between 5 and 40 μm with diameters between 0.05 and 1 μm.

A strong conclusion which can be drawn from the above experimental

Table 4-10

Tumors in Abdomen and/or Thorax After Intraperitoneal Injection of Glass Fibers, Crocidolite, or Corundum in Rats

Dust	Form[b]	I.P. Dose	Effective Number of Dissected Rats	No. of Days Before First Tumor	Average Survival Time of Rats with Tumors (days after injection)	Rats with Tumors (percent)	Tumor Type[c]					
							1	2	3	4	5	6
Glass fibers HR 104	f	2	73	421	703	27.4	17	3	-	-	1	1
Glass fibers HR 104	f	10	77	210	632	53.2	36	4	-	1	3	-
Glass fibers HR 104	f	2 x 25	77	194	367	71.4	47	6	2	-	-	-
Crocidolite	f	2	39	452	761	38.5	12	3	-	-	2	1
Corundum	g	2 x 25	37	545	799	8.1	1	-	-	2	2	2
UICC Rhodesian chrysotile	f	2	37	431	681	16.2	4	2	-	-	1	-
UICC Rhodesian chrysotile	f	6.25	35	343	501	77.1	24	3	-	-	-	-
UICC Rhodesian chrysotile	f	25	31	276	419	80.6	21	2	1	1	-	-
UICC Rhodesian chrysotile	f	4 x 25	33	323	361	54.5	16	2	-	-	-	-
UICC Rhodesian chrysotile	f	3 x 25 s.c.	33	459	449	3.0	-	-	1 s.c.	-	-	-
UICC Rhodesian milled	f	4 x 25	37	400	509	32.4	9	3	-	-	-	-
Polyonscite	f	3 x 25	34	257	348	76.5	24	2	-	-	-	-

Table 4-10 (continued)

Tumors in Abdomen and/or Thorax After Intraperitoneal Injection of Glass Fibers, Crocidolite, or Corundum in Rats[a]

Dust	Form[b]	I.P. dose	Effective Number of Dissected Rats	No. of Days Before First Tumor	Average Survival Time of Rats with Tumors (days after injection)	Rats with Tumors (percent)	Tumor Type[c]					
							1	2	3	4	5	6
Glass fibers s * s 106	f	?	34	692	692	2.9	1	-	-	-	-	-
Glass fibers S * S 106	f	10	36	350	530	11.1	2	2	-	-	1	-
Glass fibers S * S 106	f	4 x 25	32	197	325	71.9	20	3	-	-	-	-
Gypsum	f	4 x 25	35	579	583	5.7	-	-	1	1	1	-
Monalite	f	4 x 25	34	249	315	73.5	17	8	-	-	-	-
Actinolite	g	4 x 25	39	-	-	-	-	-	-	-	-	-
Biotite	g	4 x 25	37	-	-	-	-	-	-	-	-	-
Haematite (precipit.)	g	4 x 25	34	-	-	-	-	-	-	-	-	-
Haematite (mineral)	g	4 x 25	38	-	-	-	-	-	-	-	-	-
Pectolite	g	4 x 25	40	569	569	2.5	-	-	-	1	1	1
Sanidine	g	4 x 25	39	579	579	2.6	-	1	-	-	-	-
Talc	g	4 x 25	36	587	587	2.8	1	-	-	-	-	-
NaCl (control)	-	4 x 2ml	72	-	-	-	-	-	-	-	-	-

From: Pott and Friedrichs, (1972); Pott et al. (1976)

[b] f = fibrous; g = granular

[c] Tumor types are: 1 Mesothelioma; 2 Spindle cell sarcoma; 3 Polya-cell sarcoma; 4 Carcinoma; 5 Reticulum cell sarcoma; 6 Benign -- not evaluated in tumor rates

Figure 4-5

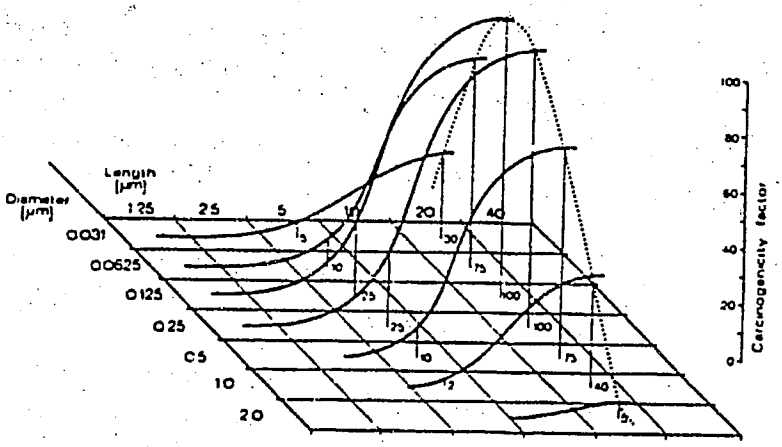

Fig. 4-5 Hypothesis concerning the carcinogenic potency of a fiber as a function of its length and width using data on tumor incidence from injection and implantation studies. From: Pott (1980)

data is that long (4 μm) and fine diameter (< 1 μm) fibers are more carcinogenic than shorter and thicker fibers when implanted on the pleura or injected into the peritoneum of animals. The origin of a reduced carcinogenicity for shorter, ball-milled fibers is less clear as the relative contributions of shorter fiber length and the significant alteration of the crystal structure by input of physical energy are not, as yet, defined. However, the extrapolation of data developed on size-dependent effects, from intrapleural or intraperitoneal administration to inhalation (where movement of the fibers in airways and subsequently through body tissues is strongly size-dependent) presents significant difficulties. Moreover, since the number of shorter (< 5 μm) fibers in an exposure circumstance may be 100 times greater than those longer, their carcinogenicity must be 100 times less before their contribution can be neglected.

4.9 Teratogenicity

There is no evidence that asbestos is teratogenic. Schneider and Maurer (1977) fed pregnant CD-1 mice doses of 4-400 mg/kg b.w. (1.43-143) for days 1 to 15 of gestation. They also administered 1, 10 or 100 μg of asbestos to day 4 blastocysts which were transferred to pseudopregnant mice. No positive effects were noted in either experiment.

4.10 Summary

The animal data on the carcinogenicity of asbestos fibers confirm and extend that epidemiological human data. Mesothelioma and lung cancer have been produced by all the principal commercial asbestos varieties, chrysotile, amosite, crocidolite and anthophyllite, even by exposures as short as one day. The deposition and clearance of fibers from the lung suggest that most (~ 99%) fibers inhaled are eventually cleared from the lung by ciliary or phagocytic action. Chrysotile appears to be more readily removed with dissolution of the fibers occurring in addition to other clearance processes. Implantation and injection studies suggest that the carcinogenicity of durable mineral fibers is

related to their dimensionality and not to their chemical composition. Long $\geq$ 4 μm and thin $\leq$ 1 μm fibers are most carcinogenic when in place at potential tumor site. However, deposition, clearance and migration of fibers is also size dependent, and the importance of all size dependent effects in the carcinogenicity of inhaled fibers is not fully established.

5. ENVIRONMENTAL EXPOSURES TO ASBESTOS

5.1 Introduction

The analysis of ambient air samples for asbestos has utilized techniques different from those used in occupational circumstances. This occurred because typical urban air may contain up to 100 $\mu g/m^3$ of particulate matter in which one is attempting to quantify asbestos concentrations from about 0.1 ng/m^3 to perhaps 1000 ng/m^3. Thus, asbestos may constitute only 0.0001 to 1 percent of the particulate matter present in a given air sample. Moreover, the asbestos found in the ambient air had a size distribution in which the vast majority of the fibers are of a length or diameter too small to be seen in an optical microscope. In many cases, these fibers and fibrils will be agglomerated with a variety of other materials present in the air samples.

The only effective method of analysis has used the electron microscope to enumerate and size all asbestos fibers (Nicholson and Pundsack, 1973; Samudra et al. 1978). Samples from such analysis were collected on Millipore(R) filters, usually with a nominal pore size of 0.8 μm and in some cases backed by a nylon mesh. To prepare a sample for analysis, a portion of the filter was ashed in a low temperature oxygen furnace, which removed the membrane filter material and all organic material collected in the sample. The residue was recovered in a liquid phase, dispersed by ultrasonification and filtered on a Nuclepore filter. The refiltered material was coated by carbon to entrap the collected particles. A segment of the coated filter was then mounted on an electron microscope grid, which, in turn, was placed on a filter paper saturated with chloroform, the vapors of which serve to dissolve the filter material. Earlier electron microscopic analysis utilized a rub-out technique in which the ash residue was dispersed in a nitrocellulose film on a microscope slide and a portion of that film mounted on an electron microscope grid for scanning purposes. Chrysotile asbestos was identified on the basis of its morphology in the electron microscope and amphiboles by their selected

area electron diffraction patterns, supplemented by energy dispersive X-ray analysis. Because of the dispersal of the fibers and their disruption by ultrasonification, no information was obtained on the size distribution of the original aerosol. Air concentrations were recorded only in terms of the total mass of asbestos present in a given air volume, usually in nanograms/m^3. (See Section 5.9 for data on the inter-convertibility of optical fiber counts and electron microscopic mass determinations.) Environmental measurements can also be made using Nuclepore(R) filters with the elimination of the ashing and refiltration steps mentioned above. However, great care must be taken to assure that fibers are not lost from the filter prior to processing.

An analysis of 25 samples collected in buildings with asbestos surfacing material, some of which showed evidence of contamination, demonstrated the inadequacy of phase contrast optical microscopic techniques for the quantification of asbestos (Nicholson et al. 1975). The Figure 5-1 shows the correlation of optical fiber counts determined using NIOSH prescribed techniques (1972) and asbestos mass measurements obtained on the same sample. In determining the fiber concentrations, all objects with an aspect ratio of 3 or greater were enumerated using phase contrast microscopy. Petrographic techniques were not utilized in order to verify whether an object was an asbestos fiber or not, as the study was designed to evaluate phase contrast microscopy. As can be seen from Figure 5-1, the optical microscopic data do not reflect the mass concentrations of asbestos determined by electron microscopy, largely because of the presence of a considerable number of nonasbestos fibers in the ambient air that are counted in the optical microscopic analysis.

5.2 General environment

Asbestos of the chrysotile variety has been found to be a ubiquitous contaminant of ambient air. A study of 187 quarterly samples collected in 48 United States cities during 1969 to 1970 showed chrysotile asbestos to be present in virtually all metropolitan areas

Figure 5-1

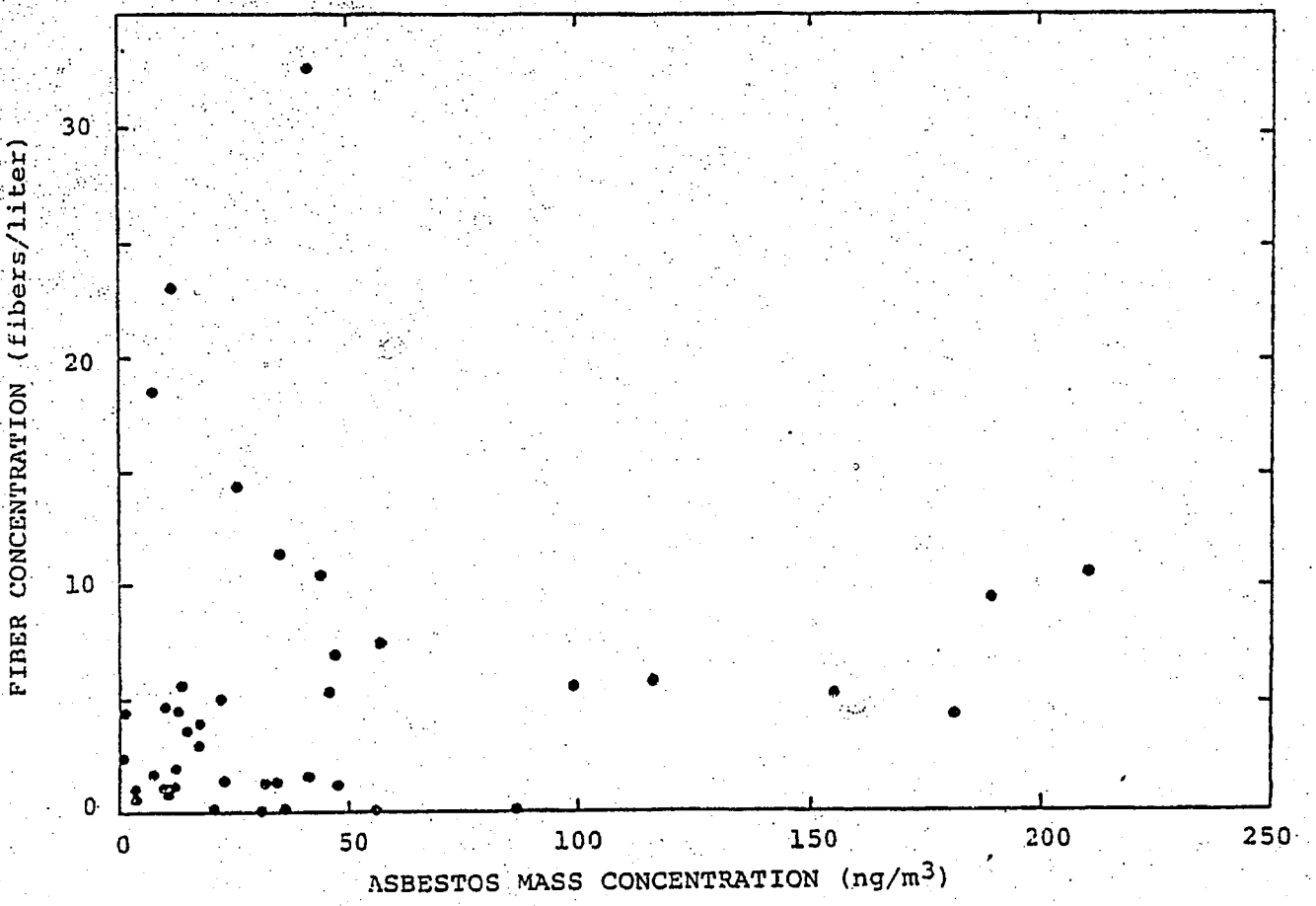

Fig. 5-1 Fiber concentrations by optical microscopy versus asbestos mass concentrations by electron microscopy.

(Nicholson, 1971; Nicholson and Pundsack, 1973). Table 5.1 lists the distribution of values obtained in that study along with similar data obtained by the Battelle Memorial Institute (EPA, 1974). Each value represents the chrysotile concentration in a composite of from five to seven 24-hour samples and, thus, averages over possible peak concentrations which could occur periodically or randomly. Of the three samples greater than 20 ng/m^3 analyzed by Mount Sinai, one was in a city having a major shipyard and another in a city that had four brake manufacturing facilities. Thus, these samples may have included a contribution from a specific source in addition to that of the general ambient air. Also shown in Table 5-1 is the distribution of chrysotile concentrations from five day samples of the air of Paris (Sebastien et al. 1980). These values were obtained during 1974 and 1975 and were generally lower than those measured in the United States, perhaps reflecting a diminished use of asbestos in construction compared to that of the U.S. during 1969-1970.

In a study of the ambient air of New York City, in which samples were taken only during daytime working hours, higher values than those mentioned above were obtained (Nicholson et al 1971). These were six-to-eight hour samples collected between 8:00 A.M. and 5:00 P.M., and reflect what could be intermittently higher concentrations during those hours compared to night time periods, for example. Table 5-2 records the chrysotile content of 22 samples collected in the five boroughs of New York and their overall cumulative distribution. It should be noted that the samples analyzed in all the studies discussed above were taken during a period when fireproofing high rise buildings by spraying asbestos-containing materials was permitted. The practice was especially common in New York City. While no sampling station was known to be located adjacent to an active construction site, unusually high levels could nevertheless have resulted from the procedure. Other sources that may have contributed to these air concentrations include automobile braking, other construction activities, consumer use of asbestos products, and maintenance or repair of asbestos-containing materials (thermal insulation, for example).

Table 5-1

The cumulative distribution of 24-hour chrysotile asbestos concentrations in the ambient air of U.S. cities and Paris, France

	Electron Microscopic Analysis				
	Mount Sinai School of Medicine[a]		Battelle Memorial Institute[b]		Paris, France[c]
Concentration (ng/m^3) less than	Number of samples	Percentage of samples	Number of samples	Percentage of samples	Percentage of samples
1.0	61	32.6	27	21.3	70
2.0	119	63.6	60	47.2	85
5.0	164	87.7	102	80.1	98
10.0	176	94.2	124	97.6	100
20.0	184	98.5	125	98.5	
50.0	185	99.0	127	100.0	
100.0	187	100.0	127	100.0	

From: [a] Nicholson, 1971; [b] EPA, 1974; [c] Sebastien, et al. 1980.

Table 5-2

Distribution of 4- to 8-hour daytime chrysotile asbestos concentrations in the ambient air of New York City 1969 - 1970

Asbestos concentration (ng/m^3) Less than	Cumulative Number of samples	Cumulative Percentage of samples
1	0	0.0
2	1	4.5
5	4	18.1
10	8	36.4
20	16	72.7
50	21	95.4
100	22	100.0

Distribution by borough

Sampling locations	Number of samples	Asbestos air level (ng/m^3) Range	Average
Manhattan	7	8-65	30
Brooklyn	3	6-39	19
Bronx	4	2-25	12
Queens	4	3-18	9
Staten Island	4	5-14	8

From: Nicholson et al., 1971

5.3 Chrysotile asbestos concentrations about construction sites

To determine if construction activities could indeed be a significant source of chrysotile fiber in the ambient air, six-to-eight hour daytime sampling was conducted in lower Manhattan in 1969 about sites where extensive spraying of asbestos-containing fireproofing material was taking place. Eight sampling sites were established about the World Trade Center construction site during the period when asbestos material were sprayed on the steelwork of the first tower. Table 5-3 shows the results of building top air samples located at sites within one-half mile of the Trade Center site and demonstrates that spray fireproofing did contribute significantly to asbestos air pollution (Nicholson et al. 1971; Nicholson and Pundsack, 1973). In some instances, chrysotile asbestos levels approximately 100 times the concentrations typically found in the ambient air were observed.

5.4 Asbestos concentrations in U.S. and French buildings

During 1974, 116 samples of indoor and outdoor air were collected in 19 buildings in 5 United States cities to assess whether contamination of the building air occurred from the presence of asbestos-containing surfacing material in rooms or return air plenums (Nicholson et al. 1975). The asbestos material in the buildings was of two main types; 1) a cementitious or plaster-like material which had been sprayed as a slurry onto steelwork or building surfaces and 2) a loosely bonded fibrous mat which had been applied by blowing a dry mixture of fibers and binders through a water spray onto the desired surface. The friability of the two types of materials differed considerably, with the cementitious spray surfaces being relatively impervious to damage while the fibrous sprays were highly friable. The results of the air sampling in these buildings are shown in Table 5.4 and provide evidence that the air of buildings with fibrous asbestos containing materials may often be contaminated.

Similar data were obtained by Sebastien et al. (1980) in a survey of asbestos concentration in buildings in Paris, France. They surveyed

Table 5-3

Distribution of 6- to 8-hour chrysotile asbestos concentrations within one-half mile of the spraying of asbestos materials on building steelwork 1969 - 1970

Asbestos concentration (ng/m^3) Less than	Cumulative Number of samples	Cumulative Percentage of samples
5	0	0.0
10	3	17.6
20	8	47.1
50	14	82.3
100	16	94.1
200	16	94.1
500	17	

Distribution of chrysotile air levels according to distance from spray fireproofing sites

Sampling locations	Number of samples	Asbestos air level (ng/m^3) Range	Average
1/8 - 1/4 mile	11	9 - 375	60
1/4 - 1/2 mile	6	8 - 54	25
1/2 - 1 mile	5	3.5 - 36	18

From: Nicholson et al., 1971

Table 5-4

The cumulative distribution of 8- to 16-hour chrysotile asbestos concentrations in buildings with asbestos-containing surfacing material in rooms or air plenums

Asbestos concentration (ng/m^3) Less than	Friable spray		Cementitious spray		Control samples	
	No. of samples	Percentage of samples	No. of samples	Percentage of samples	No. of samples	Percentage of samples
1	5	9.3	3	10.7	5	14.7
2	6	11.1	6	21.4	6	17.6
5	8	14.8	10	35.7	15	44.1
10	15	27.8	17	60.7	21	61.8
20	28	51.9	26	92.9	29	85.3
50	44	81.5	27	96.4	33	97.1
100	49	90.7	27	96.4	34	100.0
200	52	96.3	28	100.0		
500	53	98.1				
1000	54	100.0				
Arithmetic average conc.		48 ng/m^3		14.5 ng/m^3		12.7 ng/m^3

From: Nicholson et al., 1975; 1976

21 asbestos insulated buildings, 12 of which had at least one measurement higher than 7 ng/m^3, the upper limit of the outdoor asbestos concentrations measured by these workers. The distribution of the 5 day asbestos concentrations in these buildings, along with 19 outdoor samples taken at the same time is shown in Table 5-5. One particularly disturbing set of data of Sebastien, et al. is the concentrations of asbestos measured after surfacing material was removed or repaired. The average of 22 such samples was 22.3 ng/m^3. In two highly contaminated areas, however, significant reductions were measured (500-750 ng/m^3 to less than 1 ng/m^3). The importance of proper removal techniques and clean-up cannot be overemphasized.

5.5 Asbestos concentrations in U.S. school buildings

Of particular concern recently was the finding of extensive asbestos use in public school buildings (Nicholson, 1978b). Asbestos surfaces were found in more than 10% of pupil use areas in schools of New Jersey, with two-thirds of these surfaces having some evidence of damage. As these values appear typical of conditions in many other states, it has been estimated that from two to six million pupils and 100,000 to 300,000 teachers may be exposed to released asbestos fibers in schools across the nation. To obtain a measure of contamination for this use of asbestos, ten schools were sampled in the urban centers of New York and New Jersey and suburban areas of Massachusetts and New Jersey. Schools were selected for sampling because of visible damage, in some cases extensive, and thus are not typical of all schools.

Table 5.6 lists the distribution of chrysotile concentrations found in samples taken over four to eight hours in these ten schools. Chrysotile asbestos concentrations ranged from 9 ng/m^3 to 1950 ng/m^3 with an average of 217 ng/m^3. Outside air samples at three of the schools varied from 3 ng/m^3 with an average of 14 ng/m^3. In all samples but two (which measured 320 ng/m^3) no asbestos was visible on the floor of the area sampled, although surface damage was generally present near the area sampled. The highest value (1950 ng/m^3) was in a sample

Table 5-5

The cumulative distribution of 5-day asbestos concentrations in Paris buildings with asbestos containing surfacing materials

Asbestos concentration (ng/m^3) Less than	Building samples		Outdoor control samples	
	No. of samples	Percentage of samples	No. of samples	Percentage of samples
		Chrysotile		
1	57	42.2	14	73.7
2	70	51.9	16	84.2
5	92	68.1	17	89.5
10	104	77.0	19	100.0
20	117	86.7		
50	128	94.8		
100	129	95.6		
200	130	96.3		
500	132	97.8		
1000	135	100.0		
Arithmetic average conc.		25 ng/m^3		1 ng/m^3
		Amphiboles[1]		
1	112	83.0	19	100.0
2	115	85.2		
5	122	90.4		
10	125	92.6		
20	129	95.6		
50	131	97.0		
100	132	97.8		
200	133	98.5		
500	135	100.0		
Arithmetic average conc.		10 ng/m^3		0.1 ng/m^3

[1] No value reported for 104 building samples. Some materials would have contained no amphibole asbestos.

From: Sebastien et al., 1980

Table 5-6

Distribution of chrysotile asbestos concentrations in 4- to 8-hour samples taken in public schools with damaged asbestos surfaces

Asbestos concentration (ng/m^3) Less than	Number of samples	Percentage of samples
5	0	0.0
10	1	3.7
20	1	3.7
50	6	22.2
100	12	44.4
200	19	70.4
500	25	92.6
1000	26	96.3
2000	27	100.0

From: Nicholson et al., 1978

following routine sweeping of a hallway in a school with water damage to the asbestos surface. However, no visible asbestos was seen on the hallway floor. Because the schools were selected on the basis of visible damage, these results cannot be considered typical of all schools with asbestos surfaces. They do, however, illustrate the extensive contamination that can occur.

A recent study conducted under the auspices of the EPA suggests that the above New Jersey samples in schools may not be atypical (Constant, Jr. et al., 1982). Concentrations identical to those above were found in the analysis of samples collected over a five day period in 25 schools with asbestos surfacing materials. The schools were in a single district and were selected by a random procedure and not chosen because of a presence or absence of damaged material. An arithmetic mean concentration of 237 ng/m^3 was measured in 54 samples collected in rooms or areas with asbestos surfacing material. In contrast, a concentration of 8 ng/m^3 was measured in 31 samples of outdoor air taken at the same time. Of special concern, 31 samples collected in the schools with asbestos, but in areas where it was not used, showed an average concentration of 54 ng/m^3, indicating the dispersal of asbestos from the source. These data are summarized in Table 5-7.

Finally, Sawyer (1977; 1979) has reviewed a variety of data on the air concentrations, measured by optical microscopy, that have been observed in circumstances where asbestos materials in building and schools are disturbed by routine or abnormal activity. These results are shown in Table 5-8 and demonstrate that a wide variety of activities can lead to high asbestos concentrations during disturbance of asbestos surfacing material. Maintenance and renovation work, particularly, if done improperly, can lead to substantially elevated asbestos levels.

5.6 Chrysotile concentrations in the homes of workers

The finding of asbestos disease in family contacts of individuals occupationally-exposed to the fiber directs attention to air concen-

Table 5-7

Cumulative distribution of 5-day chrysotile asbestos concentrations in 25 schools with asbestos surfacing materials, 1980-1981

Asbestos concentration (ng/m^3) Less than	Rooms with asbestos		Rooms without asbestos		Outdoor controls	
	No. of samples	Percentage of samples	No. of samples	Percentage of samples	No. of samples	Percentage of samples
			Chrysotile			
1	4	7.4	6	19.3	18	58.1
2	6	11.1	7	22.6	21	67.7
5	7	13.0	10	38.7	26	83.9
10	10	18.5	12	41.9	28	90.3
20	16	29.6	13	54.8	29	93.5
50	25	46.3	17	87.1	30	96.8
100	33	61.1	27	93.5	31	100.0
200	43	79.6	29	96.8		
500	48	88.9	31	100.0		
1000	54	100.0				
Arithmetic average conc.		231 ng/m^3		54 ng/m^3		8 ng/m^3
			Amphiboles			
1	44	81.5	21	67.7	26	83.9
2	45	83.3	22	71.0	29	93.5
10	48	88.9	26	83.9	30	96.8
20	50	92.6	27	87.1	30	96.8
50	52	96.3	27	87.1	31	100.0
100	52	96.3	29	93.5		
200	53	98.1	31	100.0		
500	54	100.0				
Arithmetic average conc.		6.1 ng/m^3		8.7 ng/m^3		0.7 ng/m^3

From: Constant, Jr. et al., 1982

Table 5-8

Airborne asbestos in buildings

Friable asbestos material

Classification	Main mode of contamination	Activity description	Mean count of fibers/cm^3	n	Range or SD
Quiet, nonspecific, routine	Fallout	None	0.0	32	0.0
	Reentrainment	dormitory	0.1	NA	0.0-0.8
		university, schools	0.1	47	0.1
		offices	0.2	14	0.1-0.6
Maintenance	Contact	relamping	1.4	2	0.1
		plumbing	1.2	6	0.1-2.4
		cable movement	0.9	4	0.2-3.2
Custodial	Mixed: contact reentrainment	cleaning	15.5	3	6.7
	reentrainment	dry sweeping	1.6	5	0.7
		dry dusting	4.0	6	1.3
		bystander	0.3	3	0.3
		heavy dusting	2.8	8	1.6
Renovation	Mixed: contact reentrainment	ceiling repair	17.7	3	8.2
		track light	7.7	6	2.9
		hanging light	1.1	5	0.8
		partition	3.1	4	1.1
		pipe lagging	4.1	8	1.8-5.8
Vandalism	Contact	ceiling damage	12.8	5	8.0

From: Sawyer, 1979.

trations in the homes of such workers. Thirteen samples have been collected in the homes of asbestos mine and mill employees and analyzed for chryostile (Nicholson, et al. 1980). The workers were employed at mine operations in California and Newfoundland and did not, at the time of sampling (1973 and 1976), have access to shower facilities nor did they commonly change clothes before going home. Table 5-9 lists the concentrations range of these samples. Three samples taken in homes of non-miners in Newfoundland yielded concentrations of 32, 45 and 65 ng/m^3. In contrast, the workers' homes were much higher, pointing to the need for appropriate shower and change facilities at asbestos workplaces. As asbestos cancers have been documented in family contacts of workers, concentrations such as seen here should be viewed with particular concern.

5.7 Summary of environmental sampling

Table 5.10 summarizes those studies of the general ambient air or of specific pollution circumstances that have a sufficient number of samples for comparative analysis. The data are remarkably consistent. Average 24 hour samples of general ambient air indicate asbestos concentrations of 1 to 2 ng/m^3 (removing from consideration two U.S. samples that may have been affected by specific sources). Short-term day time samples are generally higher reflecting possible contributions of traffic, construction and other of man's activities. Of buildings with asbestos-surfacing materials, average concentrations 100 times those of the ambient air are seen in schools. Concentrations of 5 to 30 times backgrounds are seen in other building circumstances.

5.8 Other emission sources

The weathering of asbestos cement wall and roofing materials has been shown to be a source of asbestos air pollution in the analysis of air samples taken in buildings constructed of such material (Nicholson, 1978a). Seven samples taken in a school after a heavy rainfall showed asbestos concentrations from 20 to 4500 ng/m^3 (arithmetic mean = 780

Table 5-9

Distribution of 4-hour chrysotile asbestos concentrations in the air of homes of asbestos mine and mill employees

Asbestos concentration (ng/m^3) Less than	Number of samples	Percentage of samples
50	0	0.0
100	4	30.8
200	8	61.5
500	10	76.9
1000	12	92.3
2000	12	92.3
5000	13	100.0

From: Nicholson et al., 1980

Table 5-10

Summary of environmental asbestos sampling

Sample set	Collection period	Number of samples	Mean concentration
Quarterly composites of 5-7 24 hour U.S. samples	1969-70	187	3.3 C
5 day samples of Paris, France	1974-75	161	0.96 C
6-8 hour samples of New York City	1969	22	16 C
5 day, 7 hour control samples for U. S. school study	1980-81	31	9 (8C,1A)
16 hour samples of 5 U.S. cities	1974	34	13 C
N.J. schools with damaged asbestos surfacing materials in pupil use areas	1977	27	217 C
U.S. school rooms/areas with asbestos surfacing material	1980-81	54	237 (231C,6A)
U.S. school room/areas in buildings with asbestos surfacing material	1980-81	31	63 (54C,9A)
Buildings with asbestos materials in Paris, France	1976-77	135	35 (25C,10A)
U.S. buildings with friable asbestos in plenums or as surfacing material	1974	54	48 C
U.S. buildings with cementitious asbestos material in plenum or as surfacing material	1974	28	15 C

C = chrysotile
A = amphibole

* Average concentration omitting two samples which may have reflected a contribution of specific sources.

ng/m^3 -- all but two exceeded 100 ng/m^3). The source was attributed to asbestos washed from asbestos cement walkways and asbestos cement roof panels. No significantly elevated concentrations were observed in a concurrent study of houses constructed of asbestos cement materials. Roof water runoff from the homes landed on the ground and was not reentrained, while that of the schools fell to a smooth walkway allowing easy reentrainment, when dry. Contamination from asbestos cement siding has also been documented by Spurny et al. (1980).

One of the more significant remaining contributions to environmental asbestos concentrations may be emissions from braking by automobiles and other vehicles. Measurements of brake and clutch emissions revealed that, annually, 2-1/2 tons of unaltered asbestos are released to the atmosphere and an additional 68 tons fall to roadways, some of which would be dispersed by passing traffic (Jacko et al. 1973).

5.9 Interconvertibility of fiber and mass concentrations

All data, scant as they are, that relate asbestos disease to exposure are derived from studies of workers exposed in occupational environments. In these studies, concentrations of fibers longer than 5 μm were determined using optical microscopy or were estimated from optical microscopic measurements of total particulate matter. On the other hand, all current measurements of low-level environmental pollution utilize electron microscopic techniques which determine the total mass of asbestos present in a given volume of air. To extrapolate dose-response data obtained in studies of working groups to environmental exposures, it is necessary to establish a relationship between optical fiber counts and mass of asbestos determined by electron microscopy.

Some data exist that relate optical fiber counts (longer than 5 μm) to the total mass of asbestos as determined by electron microscopic techniques or other weight determinations. These are listed in Table 5-11 and provide crude estimates of a conversion factor relating fiber concentrations (f/ml) to airborne asbestos mass (μg/m^3). The proposed

Table 5-11

Measured Relationships Between Optical Fiber Counts and Mass of Airborne Chrysotile

Sampling Situation	Fiber[a] Counts (f/ml)	Mass Concentration ($\mu g/m^3$)	Conversion Factors $\frac{\mu g/m^3}{f/ml}$ or $\frac{\mu g}{10^6 f}$	$10^3 f/mg$
Textile factory BOHS (1968) (weight vs. fiber count)	2	120	60	16
Air chamber monitoring Davis, et al. (1978)	1,950	10,000	5	200
Monitoring brake repair work Rohl, et al. (1976) (T.M. mass vs. fiber count)	0.1 to 4.7 (7 samples)	0.1 to 6.6	0.7 to 24[b] mean = 6	170
Textile mill			150[c]	6.7
Friction products mfg.			70[c]	13.9
Pipe mfg. Lynch, et al. (1970)			45[c]	22.5

[a]All fiber counts used phase-contrast microscopy and enumerated fibers longer than 5 μm.

[b]Conversion factor may be low due to losses in E.M. processing.

[c]Conversion factor may be high because of overestimate of asbestos mass on the basis of total magnesium.

standards for asbestos in Great Britain by the British Occupational Hygiene Society (BOHS) stated that a "respirable" mass of 0.12 mg asbestos/m^3 was equivalent to 2 f/ml (BOHS, 1968). It was not stated how this relationship was determined. However, if it were from magnesium determinations in an aerosol, the weight determination would likely be high because of the presence of other nonfibrous, magnesium-containing compounds in the aerosol. Such was the case in the work of Lynch, et al. (1970), and their values for the conversion factor are undoubtedly overestimates. The data of Rohl, et al. (1976) are likely to be underestimates because of possible losses in the determination of mass by electron microscopy. No information exists on the procedures used to determine the mass of chrysotile in the data presented by Davis, et al. (1978).

The range of 5 to 150 for the conversion factor relating mass concentration to optical fiber concentration is great, and any average value derived from it has a large uncertainty. However, for the purpose of extrapolating to low mass concentrations from fiber count, the geometric mean, 30 $\mu g/m^3$/f/ml, of the above range of conversion factors will be used. The geometric standard deviation of this value is 4 and this uncertainty severely limits any extrapolation in which it is used. In the case of amosite, the data of Davis, et al. (1978) suggest that a conversion factor of 18 is appropriate. However, since this data yielded lower chrysotile values than all other chrysotile estimates, it may also be low for amosite.

5.10 Summary

Measurements using electron microscopic techniques have established the presence of asbestos in the urban ambient air, usually at concentrations less than 10 ng/m^3. Concentrations of from 100 ng/m^3 to 1000 ng/m^3 have been measured near specific asbestos emission sources, in schools where asbestos-containing materials are used for sound control, and in office buildings where similar materials are used for fire control.

6. RISK EXTRAPOLATIONS AND HUMAN EFFECTS OF LOW EXPOSURES

6.1 Risk extrapolations for lung cancer and mesothelioma

In order to obtain dose-response estimates at current or projected environmental asbestos concentrations, it is necessary to extrapolate from epidemiological data on deaths that have resulted from exposures to the considerably higher concentrations extant in occupational circumstances. As mentioned previously, the available data are compatible with a linear exposure-response relatioship, with no evidence of a threshold. However, the limited data indicating the validity of this relationship are for exposures two or three orders of magnitude higher than those of concern for environmental exposures.

The range of values determined for K_L and K_M in Chapter 3 will be used to calculate a range of risks from daytime exposure to 0.01 f/ml. This concentration corresponds to about 300 $\mu g/m^3$, a concentration previously found in several environmental exposure circumstances.

Tables 6-1 and 6-2 list a range of calculated lifetime risks of mesothelioma and lung cancer for a 40 hr/wk exposure to 0.01 f/ml for various time periods. Values of $K_L = 0.3$ to 3×10^{-2} and values of $K_M = 0.3$ to 3.0×10^{-8}, were used in these calculations. 1977 United States mortality rates were utilized as the basic data for the calculation. We considered that current U.S. male rates reflected the experience of 67% smokers and exsmokers and current female rates the experience of 50% smokers. Using these percentages and the data of Hammond on the mortality ratio of smokers to nonsmokers, smoking specific total mortality rates were calculated. Current U.S. rates for lung cancer were used to represent the effect of cigarette smoking in males. The current female rates were doubled to reflect the rapid increase in female lung cancer risk. Nonsmoking lung cancer rates for both males and females were taken from Garfinkel (1981). The results show the importance of the time course of mesothelioma. Children exposed at younger ages are especially susceptible because of their long life expectancy. The time of exposure plays little role in the

Table 6-1

The range of lifetime risks per 100,000 females of death from mesothelioma and lung cancer from an asbestos exposure of 0.01 f/ml for 40 hours/wk according to age, duration of exposure and smoking

Age at onset of exposure	Years of exposure 1	5	10	20
	Mesothelioma in Female Smokers			
0	1.0 - 9.9	4.6 - 45.7	8.2 - 82.2	13.3 - 133.0
10	0.6 - 6.4	2.9 - 28.8	5.1 - 51.0	8.0 - 80.0
20	0.4 - 3.8	1.7 - 16.8	2.9 - 29.1	4.4 - 43.8
30	0.2 - 2.0	0.9 - 8.8	1.5 - 14.7	2.1 - 21.0
50	0.04 - 0.4	0.1 - 1.4	0.2 - 2.1	0.3 - 2.5
	Lung Cancer in Female Smokers			
0	0.1 - 1.3	0.6 - 6.4	1.3 - 12.7	2.5 - 25.4
10	0.1 - 1.3	0.6 - 6.4	1.3 - 12.7	2.5 - 25.4
20	0.1 - 1.3	0.6 - 6.4	1.3 - 12.7	2.5 - 25.0
30	0.1 - 1.3	0.6 - 6.3	1.2 - 12.3	2.3 - 22.8
50	0.09 - 0.9	0.4 - 4.2	0.7 - 7.4	1.1 - 10.8
	Mesothelioma in Female Nonsmokers			
0	1.1 - 10.6	4.8 - 48.7	8.8 - 87.7	14.2 - 142.4
10	0.7 - 6.8	3.1 - 31.0	5.8 - 58.0	8.7 - 86.6
20	0.4 - 4.1	1.8 - 18.3	3.2 - 31.7	4.8 - 48.0
30	0.2 - 2.2	1.0 - 9.7	1.6 - 16.4	2.4 - 23.5
50	0.04 - 0.4	0.2 - 1.6	0.2 - 2.4	0.3 - 2.9
	Lung Cancer in Female Nonsmokers			
0	0.02 - 0.2	0.09 - 0.9	0.2 - 1.9	0.4 - 3.7
10	0.02 - 0.2	0.09 - 0.9	0.2 - 1.9	0.4 - 3.8
20	0.02 - 0.2	0.09 - 0.9	0.2 - 1.9	0.4 - 3.7
30	0.02 - 0.2	0.09 - 0.9	0.2 - 1.9	0.4 - 3.6
50	0.02 - 0.2	0.08 - 0.8	0.2 - 1.5	0.3 - 2.5

Table 6-2

The range of lifetime risks per 100,000 males of death from mesothelioma and lung cancer from an asbestos exposure of 0.01 f/ml for 40 hours/wk according to age, duration of exposure and smoking

Age at onset of exposure	Years of exposure 1	5	10	20
	Mesothelioma in Male Smokers			
0	0.8 - 7.6	3.5 - 34.5	6.2 - 61.1	9.8 - 98.2
10	0.5 - 4.7	2.1 - 21.0	3.7 - 36.8	5.6 - 55.6
20	0.3 - 2.6	1.2 - 11.7	2.0 - 20.0	2.9 - 29.4
30	0.1 - 1.4	0.6 - 5.8	1.0 - 9.6	1.3 - 13.2
50	0.02 - 0.2	0.08 - 0.8	0.1 - 1.1	0.1 - 1.3
	Lung Cancer in Male Smokers			
0	0.2 - 2.0	1.0 - 9.9	2.0 - 19.9	4.0 - 39.7
10	0.2 - 2.0	1.0 - 10.0	2.0 - 20.0	4.0 - 39.9
20	0.2 - 2.0	1.0 - 10.1	2.0 - 20.1	4.0 - 39.7
30	0.2 - 2.0	1.0 - 10.1	2.0 - 20.0	4.0 - 37.7
50	0.2 - 1.7	0.8 - 7.7	1.4 - 13.5	1.9 - 19.2
	Mesothelioma in Male Nonsmokers			
0	0.9 - 8.9	4.1 - 40.7	7.3 - 73.1	11.8 - 117.5
10	0.6 - 5.6	2.5 - 25.2	4.5 - 44.7	7.0 - 69.5
20	0.3 - 3.2	1.5 - 14.6	2.5 - 25.1	3.7 - 37.4
30	0.2 - 1.7	0.8 - 7.5	1.3 - 12.5	1.8 - 17.6
50	0.03 - 0.3	0.1 - 1.1	0.2 - 1.6	0.2 - 1.9
	Lung Cancer in Male Nonsmokers			
0	0.02 - 2.1	0.1 - 1.1	0.2 - 2.1	0.4 - 4.2
10	0.02 - 2.1	0.1 - 1.1	0.2 - 2.1	0.4 - 4.2
20	0.02 - 2.1	0.1 - 1.1	0.2 - 2.1	0.4 - 4.2
30	0.02 - 2.2	0.1 - 1.1	0.2 - 2.1	0.4 - 4.1
50	0.02 - 2.0	0.1 - 0.9	0.2 - 1.6	0.3 - 2.8

lifetime excess risk of lung cancer; any exposure before the age of 45 or 50 contributes equally to the lifetime risk. It must be emphasized that the risk estimates are uncertain because of the variability of the data from which values of K_L were calculated. Thus, actual risks in a given environmental exposure could be outside the listed ranges.

6.2 Observed environmental asbestos disease

Asbestos-related disease in persons who had not been directly exposed at the workplace has been known since 1960. In that year Wagner et al. published a review of 47 cases of mesothelioma found in the North-west Cape Province of South Africa in the previous five years. Approximately half the cases described were in individuals who had, decades before, simply lived or worked near an area of asbestos mining. The hazard from environmental asbestos exposure was further documented in the findings of Newhouse and Thomson, who showed that mesothelioma could occur among individuals whose potential asbestos exposure consisted of having resided near an asbestos factory or in the household of an asbestos worker. Twenty of 76 cases from the files of the London Hospital were the result of such exposures.

Of considerable importance are the data forthcoming on the prevalence of X-ray abnormalities and the incidence of mesothelioma in family contacts of the amosite factory employees in Paterson, New Jersey. Anderson and Selikoff (1979) have shown that 35% of 685 family contacts of former asbestos factory workers had abnormalities characteristic of asbestos exposure, when X-rayed 30 or so years after first household contact. The data are shown in Table 6-3, which compares the household group with 326 New Jersey urban residents. The overall difference in the percentage of abnormalities between the two groups is highly significant. Of special concern was the finding that the difference in the prevalence of abnormalities in a group of children born into a worker's household after his employment ceased was also significant.

Table 6-3

Prevalence of radiographic abnormalities associated with asbestos exposure among household members of amosite asbestos workers

Exposure group	Total examined	One or more radiographic abnormalities present*	
New Jersey urban residents**	326	15 (5%)	$\chi^2 = 7.1$ $p < .01$
Entered household after active worker employment ceased†	40	6 (15%)	
Household resident during active worker employment†	685	240 (35%)	$\chi^2 = 6.8$ $p < .01$
Household resident and personal occupational asbestos exposure	51	23 (45%)	

* ILO U/C Pneumoconiosis Classification categories: irregular opacities 1/0 or greater; pleural thickening; pleural calcification; pleural plaques.

** No known direct occupational or household exposure to asbestos.

† No known direct occupational exposure to asbestos.

A matched comparison group: chest x-ray abnormalities among 685 household contacts of amosite asbestos workers and 326 individual residents in urban New Jersey

Group	Total examined	Pleural thickening present	Pleural calcification present	Pleural plaques present	Irregular* opacities present
Household contacts of asbestos workers	685	146 (18.8%)	66 (8.5%)	61 (7.9%)	114 (16.6%)
Urban New Jersey residents	326	4 (1.2%)	0 (8.5%)	2 (0.6%)	11 (3.4%)

* ILO U/C Pneumoconiosis Classification irregular opacities 1/0 or greater.

Through 1977, four deaths from mesothelioma have occurred among the family contacts of these same factory workers. Table 6-4 lists the cases by time from onset of exposure along with the number of deaths from other causes in the same time period (1961-1977; one death occurred subsequent to 1977). As can be seen, 1% of deaths after 20 years from first exposure were from mesothelioma; however, further observations will be necessary to fully establish the incidence of this neoplasm among family contacts. An additional contribution of asbestos-related lung cancer could also exist, but studies in this regard have not yet been completed.

A second population-based mortality study of mesothelioma (and other cancer) risks in environmental circumstances is that of Hammond et al. (1979b). The study compared the mortality of a group of 1,779 residents within one-half mile of the Paterson amosite asbestos plant with 3,771 controls in a different, but economically similar section of town. No differences in the relative mortality experiences were seen, except for one mesothelioma in the neighborhood group. This one case was in an electrician and an occupational exposure may have been contributory.

6.3 Comparison of observed mortality with extrapolated data

The mortality data in these two population-based studies can be compared with estimates from the data that led to Table 6-4 (but calculated for 35 years, rather than a lifetime) and adjusted to a continuous rather than daytime exposure). If the air concentration in both circumstances was 200 ng/m^3, approximately 2 mesothelioma deaths/100,000 would be expected in the 35 years. In both cases, the exposed population was about 2,000, so the expected number of mesotheliomas would be 0.04 (range, 0.004-0.4).

The higher numbers observed, particularly in the household group, would suggest that higher exposures (as from shaking dusty overalls) may have occurred in workers' homes, or that the extrapolations based on occupational data may understate risks.

Table 6-4

Mesothelioma following onset of factory asbestos exposure, 1941-1945

	Factory workers (933)		Household contacts (2205)	
Years from onset	Total deaths	Mesothelioma	Total deaths	Mesothelioma
< 20 years	270	0	280	0
20-24 years	102	2	93	0
25-29 years	113	5	111	0
30-34 years	84	7	124	3
35+ years	5	0	56	1
Total > 20 years	304	14	384	4
Total all years	574	14	664	4

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